

Attorney Docket No.: 930008-2202 (BOE0003US.NP)
Inventors: Klokke et al.
Serial No.: 10/541,894
Filing Date: December 2, 2005
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REMARKS

Claims 24-48 are pending in the instant application. Claims 24-48 have been rejected. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Objections to the Specification

The specification has been objected to for failing to appropriately denote trademarks. Accordingly, Applicants have amended the specification at pages 9-13 to denote the trademarks therein in capital letters. It is therefore respectfully requested that this objection be reconsidered and withdrawn.

II. Rejections Under 35 U.S.C. §102

Claims 24-31, 34-35, 38, 40-43 and 45-48 have been rejected under 35 U.S.C. 102(b) as being anticipated by Price et al. (US 4,128,658). It is suggested that Price et al. teach a method of producing oral sustained release tablets, wherein the active ingredient, anhydrous lactose and most of the Cutina HR (a hydrogenated castor oil) are intimately mixed and then the mixture is moistened by mixing with a 10% solution of the remainder of the Cutina HR ... the moistened mass is granulated through a 1.2 mm aperture sieve and dried at 50°C in a fluidised bed dryer. It is suggested that this reference teaches that the granules are then passed through a 0.85 mm aperture sieve, blended with the magnesium stearate and compressed ... on a tableting machine with 12.5 mm diameter punches (Col. 29, Example c, lines 29-47). The Examiner suggests that in another exemplified preparation (for an oral syrup), the drug is

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dissolved in water (Col. 29, line 56), wherein because the drug dissolves in water it is inherently hydrophilic. It is suggested that Price et al. also teach the limitations set forth in claims 25-27, 29-31, 34-35, 38, 40, 42-43 and 45-48 at Col. 29, Example c, lines 29-47. It is further suggested that the limitations set forth in claim 28 are taught by Price et al. at Col. 29, line 56. Applicants respectfully traverse this rejection.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). MPEP 2131.

In this case, the Examiner has primarily relied on Example (c) at column 29 of Price et al. as a basis for rejection the present claims. However, Applicants respectfully submit that this example fails to disclose all the features of claims 24, 41, and 46 and by dependency claims 25-31, 34-35, 38, 40, 42-43, 45, and 47-48.

Specifically, claim 24 (and similarly claims 41 and 46) recites "...wetting a mixture of one or more active ingredients and one or more retarding agents with an oily substance..." however, example (c) of Price et al. does not disclose the use of any *oily substance* to wet the granulation mixture. Applicants assume from the wording in the Office Action and the rejection of claims 34-35 that the Examiner believes that the "10% solution of ... Cutina HR in Industrial Methylated Spirit OP 74" is an "oily substance." However, it is respectfully submitted that such a solution of Cutina HR would not fall within the literal definition of an "oily substance." Moreover, as is clear from the teachings at the

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bottom of page 9 of the present specification, the term "oily substance" does not include such solutions of Cutina HR. Indeed, while page 9 of the present specification discloses the possible use of castor oil (a liquid at room temperature) as a suitable oily substance, this passage makes no reference to the use of solid, hydrogenated, castor oil (i.e., Cutina HR) in any form of solution, let alone in Industrial Methylated Spirit OP 74.

Thus, contrary to the Examiner's suggestion that Price et al. teach the present invention, this reference does not in fact expressly or inherently describe each and every element of claims 24, 41, and 46, and all claims dependent thereon. Therefore, it is respectfully requested that this rejection under 35 U.S.C. 102(b) be reconsidered and withdrawn.

III. Rejections Under 35 U.S.C. §103

Claims 32-33, 36-37, 39 and 44 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Price et al. (US 4,128,658) in view of Santus et al. (US 5,472,704). The Examiner acknowledges that Price et al. do not expressly teach the combination of the lipophilic retarding agent with a hydrogel matrix forming agent or a structural matrix forming agent. However, it is suggested that Santus et al. teach bioadhesive granules with matrix units for the controlled release of furosemide (Col. 8, lines 63-64, Example 1). It is suggested that this reference teaches that a hydrophobic matrix is obtained by granulation with melted excipients (Col. 8, lines 66-67). The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of producing granules with an active ingredient

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and a lipophilic retarding agent, as suggested by Price et al. and combine the same with the method of producing granules of active ingredients with a lipophilic retarding agent in combination with acrylic copolymer and hydroxypropylmethylcellulose, as taught by Santus et al. and produce the instant invention. Regarding claims 32-33, 36-37, 39, and 44, it is suggested that the limitations recited in these claims would have been obvious modifications of the teachings in the cited prior art. Applicants respectfully traverse these rejections.

As discussed above, Price et al. fail to teach the use of an "oily substance" to wet a granulation mixture. Moreover, given the properties of Cutina HR, the claimed invention would not be achieved. Specifically, as indicated in the Declaration by Dr. Ina Otto submitted herewith, the Cutina HR would precipitate on the surface of the granules as the solvent evaporates. Although this may provide a sufficient mechanism for getting additional retarding agent into the mixture, the uneven coating of the precipitated Cutina HR on the granules would have no significant effect in negating undesirable properties of the active ingredient in the particles, e.g., their hydrophilic or corrosive properties.

In contrast, the use of the "oily substance" of the present invention ensures that the active ingredient particles are entirely coated, thus completely negating the undesirable properties of the particles, which would otherwise have an adverse effect on either the manufacturing process, the machinery used, or both. See the passage spanning pages 7 and 8 of the present specification. Moreover, as indicated in this passage,

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the uniform oily coating leads to especially good embedding of the active ingredient(s).

Thus, the oily substance of the present invention has an entirely different effect than the Cutina HR solution of the prior art, which simply acts as a vehicle for delivering further quantities of Cutina HR into the mixture.

MPEP 2143 indicates that in order to support a *prima facie* case of obviousness, all the claimed elements must have been known in the prior art such that one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. *KSR*, 550 U.S. at ___, 82 USPQ2d at 1395; *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); *Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp.*, 340 U.S. 147, 152, 87 USPQ 303, 306 (1950). In so far as there is no teaching in the cited prior art of using an oily substance in a granulation process, the combined teachings of the cited references fail to make the present invention obvious. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

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favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Jane Massey Licata

Jane Massey Licata
Registration No. 32,257

Date: May 5, 2008

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Examiner: Aradhana Sasan
Customer No.: 26259
Group Art Unit: 1615
Confirmation No.: 6226
Title: Granulate Comprising an Oily Substance,
Corresponding Production Method and
Tablet

Electronically submitted via EFS-Web

Date: May 5, 2008

I hereby certify that this paper is being electronically
Submitted on the date indicated above to the
Commissioner for Patents, U.S. Patent and
Trademark Office.

By Jane Massey Licata
Typed Name: Jane Massey Licata, Reg. No. 32,257

Commissioner for Patents
U.S. Patent and Trademark Office

DECLARATION

I, Dr. Ina Otto, do hereby declare and say as follows:

1. I am pharmacist, having a PHD in Pharmaceutical Technology. At the moment I am Group Head in Pharmaceutical Development of solid dosage forms at HEXAL AG, Holzkirchen Germany.



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2. I have reviewed the Office Action issued in this case dated December 5, 2007. I have further reviewed and am familiar with the Example (c) at column 29 of U.S. Patent No. 4,128,658, (Price et al.) as identified by the Examiner in the Office Action.

3. CUTINA HR is solid, hydrogenated castor oil used as a retardation component and pressing agent for the preparation of tablets for pharmaceutical application.

4. When used as described in Example (c) at column 29 of Price et al., a "10% solution of ... Cutina HR in Industrial Methylated Spirit OP 74" would precipitate on the surface of the granules as the solvent evaporates, thereby providing further quantities of Cutina HR onto the surface. Although this may provide a sufficient mechanism for getting additional retarding agent into the mixture, the uneven coating of the precipitated Cutina HR on the granules would have no significant effect in negating undesirable properties of the active ingredient in the particles, e.g., their hydrophilic or corrosive properties.

I hereby declare that all statements herein of our own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements were made with the knowledge that willful statements and the like so made are punishable by fine or by imprisonment, or both, under '1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application, any patent issuing there upon, or any patent to which this verified statement is directed.

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Dr. Ina Otto

Date

29.10.2005

